

**REMARKS**

**I. Status of Claims**

Applicants have added new claims 14-20. Claims 2 and 5-6 were cancelled by earlier amendments. Upon entry of this amendment, claims 1, 3, 4, and 7-20 will be pending and under examination.

Support for new claims 14-20 can be found throughout the application, including, for example, paragraphs [0031]-[0033], [0044], and [0046] of the published application (U.S. Patent Application Publication No. 2006/0234241), and the original claims. Accordingly, these amendments do not add new matter and Applicants respectfully request their entry.

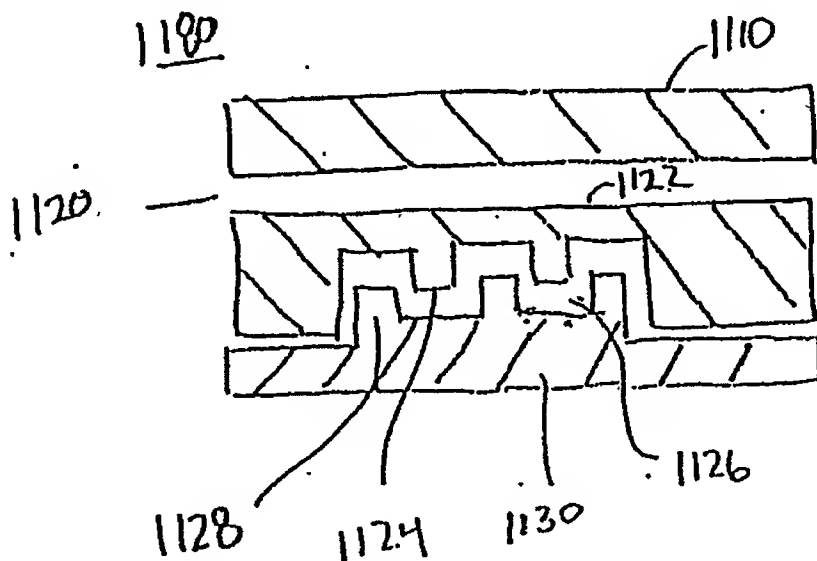
**II. Rejections under 35 U.S.C. § 102(b)**

Claims 1, 3-4, and 7-13 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by International Publication No. WO 02/40874 by Quake *et al.* (*Quake*). According to the Office, *Quake* discloses a first substrate and a second substrate connected to the first substrate defining a connection surface, wherein the substrates are grooved forming a channel and wherein the grooves have projections forming a gap, wherein the gap is variable by moving the projections, and wherein the gap is configured to block beads of a size greater than the gap. Office Action at 3. The Examiner also cites to portions of *Quake* that allegedly disclose the features of claims 3, 4, and 7. The Examiner, however, does not address the additional features of claims 8-13, which were included in the rejection. Applicants traverse.

Anticipation requires that a single reference teach every limitation of a claim.

M.P.E.P. § 2131; see also *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.").

*Quake* does not teach all elements of claim 1, from which the remaining rejected claims depend. For example, *Quake* does not teach a first and second substrate defining a connecting surface therebetween, the substrates defining a *microchannel in the connecting surface* by a first groove part of the first substrate and a second groove part of the second substrate, where the grooves include protruding parts to define a gap part of the microchannel. The Examiner's rejection appears to be based on Figure 11C of *Quake* and the description of it in paragraph 208 of *Quake*. For the Examiner's convenience, Applicants include a reproduction of Figure 11C of *Quake* here.



Paragraph 208 of *Quake* explains that feature 1122 in Figure 11C is a *membrane* between two channels (1120 and 1126) and therefore not does not define a *microchannel in a connecting surface between two substrates*. See, e.g., lines 24-26 on page 47 of *Quake* (“[t]hus, the membrane 1122 between the control 1120 and branch flow channels 1126 includes elastomeric protrusions 1124 as does the section 1130 of the branch flow channel opposing the membrane (i.e., protrusions 1128)”). Accordingly, for at least this reason, *Quake* does not teach all the features of claim 1 and does not anticipate it. Claims 3, 4, and 7-13 all depend from claim 1 and are not anticipated due at least to their dependency.

Applicants further submit that *Quake* also fails to teach the feature of claim 3, which recites that the first and second protruding parts are opposed. The Examiner cites to paragraph 208, lines 24-30 of *Quake*, which merely indicates that the *membrane* 1126 is opposed to section 1130 of the branch flow channel—i.e., *Quake* does not teach (or suggest) that the *protrusions* themselves are opposing, as recited in claim 3. Thus, for this additional reason, *Quake* does not anticipate claim 3.

With regard to claims 8-13, Applicants reiterate that the Examiner has not alleged that *Quake* teaches the features recited in these claims. Accordingly, Applicants are under no obligation to address the rejection of claims 8-13 under 35 U.S.C. § 102(b) further. See, e.g., 37 C.F.R. § 1.104(c)(2) (“[t]he pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified.”).

Applicants respectfully request withdrawal of this rejection.

### III. Rejections under 103

#### A. Quake, in view of Lough or Smith

Claims 8-12 stand rejected over *Quake* in view of U.S. Patent No. 5,900,481 to Lough *et al.* (*Lough*) or U.S. Patent No. 6,270,970 to Smith *et al.* (*Smith*). The Examiner relies on *Quake* as described in the rejection under 35 U.S.C. § 102(b), above, and acknowledges that “*Quake* is silent regarding the size, structure, or composition of the beads.” Office Action at 4. These deficiencies are allegedly remedied by *Lough* or *Smith*. In particular, the Examiner alleges that the skilled artisan would be motivated to combine *Lough* with *Quake* “based on the preferred differential immobilization of *Lough* (Abstract).” *Id.* at 5. The Examiner further alleges that the skilled artisan would be motivated to apply the chaotropic salts of *Smith* to the device of *Quake* “for the expected benefit of providing unfolded nucleic acids that are more thermodynamically stable...[to] favor hybrid formation.” *Id.* Applicants traverse.

When asserting an obviousness rejection, the Examiner must base the rejection on the claims as a whole, considering all claim features, and not merely the differences between the claims and cited references. See M.P.E.P. §§ 2141.02 (I) and 2143.03. Furthermore, “rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR International Co. v. Teleflex Inc.*, 82 U.S.P.Q. 2d 1385, 1396 (2007), quoting *In re Kahn*, 78 U.S.P.Q. 2d 1329, 1336 (Fed. Cir. 2006); see also M.P.E.P. §§ 2141(II), 2142. The KSR Court

further noted that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 82 U.S.P.Q. 2d at 1389. Moreover, modifying or combining references in an obviousness rejection requires a reasonable expectation of success. See M.P.E.P. § 2143.02(II).

Applicants respectfully submit that the Examiner has not fully considered the claims as a whole, or the teachings of the references cited against them. In addition, the motivation suggested by the Examiner to combine the cited art is largely conclusory and essentially based on Applicants' teachings. See M.P.E.P. § 2141.01, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) ("It is difficult but necessary that the decisionmaker forget what he or she has been taught...about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art.").

As discussed under the previous heading, *Quake* does not teach or fairly suggest the feature of a microchip comprising a microchannel in the connecting surface of the first and second substrates of the microchip. Instead, *Quake* merely describes a membrane between flow and control channels, which is neither a teaching or fair suggestion of a *microchannel in the connecting surface*. *Lough* and *Smith* do not remedy this deficiency of *Quake*, since, *inter alia*, these references do not describe microchannel-containing devices.

In addition, the proffered motivation to combine *Quake* with *Lough* or *Smith* is conclusory. The Examiner has not articulated an adequate basis for why the skilled artisan considering *Quake* would look to *Lough* or *Smith* to specify the size, structure, or composition of particles, or the use of chaotropic agents—absent Applicants' teachings. Instead, the Examiner cites to a vague reference to “preferred differential immobilization” in *Lough* and alleged thermodynamic stability of denatured nucleic acids for hybridization from *Smith* to support the rejection. These supposed teachings of *Lough* and *Smith*, however, do not provide a basis for why the skilled artisan would modify *Quake*—even assuming that *Quake* otherwise taught the features of claim 1, which Applicants do not concede.

To the extent that this rejection might be applied to the newly added claims, Applicants note that the cited references fail to teach or suggest the further feature of a microchannel where the inner wall surface has been coupled with a silane coupling agent comprising a trialkyl halogenosilane, as recited in, e.g., claims 14, 19, and 20. The present application, in contrast, teaches that surface treatment advantageously prevents the buildup of dust, which impairs microchip sensitivity and performance. See, e.g., paragraphs [0043]–[0045] of the published application. The problem of dust is particularly pernicious for microchannels, which, unlike flat surfaces, cannot be easily washed out. See *id.*

To illustrate this problem, the present application demonstrates that surface treatment with a trialkyl halogenosilane, such as triethylchlorosilane, does not produce dust (e.g., from polymerization of the silane) at concentrations of 10%. In contrast,

octadecyltrichlorosilane at a concentration of only 5% produced dust in the microchannel. In short, the cited references, alone or in combination, do not teach or fairly suggest the advantage of using trialkyl halogenosilanes to surface treat the inside of microchannels in the microchips provided by the invention.

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection.

B. *Zenhausen* in view of *Quake* and *Lough* or *Smith*

Claims 1, 3-4, and 7 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent Application Publication No. 2004/0011650 by *Zenhausen et al.* (*Zenhausen*) in view of *Quake*. Office Action at 6. According to the Office, *Zenhausen* describes a microchip with a microchannel containing a moveable array of constrictions formed in a substrate. The Office acknowledges, however, that *Zenhausen* “does not specifically teach a channel formed between two grooved substrates...[or] a size of the particle relative to the constriction.” *Id.* The Examiner cites to *Quake* to remedy these deficiencies, alleging that *Quake* describes one of “the variety of known techniques to construct the channels.” *Id.* The Examiner further alleges that the skilled artisan would be motivated to combine these references, based on “the benefit of facilitating retention and analysis of analytes on the particles as taught by *Quake*”—although the Examiner offers no explanation for *why* this supposed benefit disclosed in *Quake* is relevant to the noted deficiency of *Zenhausen*, *i.e.*, *Zenhausen*’s failure to describe a microchannel formed by grooves in the two substrates. *Id.* at 7.

Claims 8-12 were rejected in further view of *Lough* or *Smith*, which were relied on as described in the previous subheading.

Applicants traverse. This rejection should be withdrawn for at least the reason that *Quake* does not teach or fairly suggest the acknowledged deficiencies of *Zenhausen*. In particular, Applicants reiterate that *Quake* merely describes a *membrane* between flow and control channels and would not teach or suggest a *microchannel in the connecting surface*, formed by grooves in the two substrates. Thus, *Zenhausen*, alone or in combination with *Quake*, does not teach or suggest all the features of the claimed invention and would not render it obvious. *Lough* and *Smith* do not remedy these deficiencies for at least the reason that neither reference describes microchannel-containing devices. Accordingly, Applicants courteously solicit withdrawal of the rejection.



**CONCLUSION**

In view of the foregoing remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

Please grant any extension of time required to enter this Amendment and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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